517,157

PCT/EP2003/014902

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Brt/V/13/02	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2003/014902	International filing date (*day/month/year*) 24 December 2003 (24.12.2003)	Priority date (*day/month/year*) 30 December 2002 (30.12.2002)
International Patent Classification (IPC) or national classification and IPC A61K 31/381, 9/70		
Applicant SCHWARZ-PHARMA AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 July 2004 (06.07.2004)	12 August 2004 (12.08.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/014902

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-17, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages 1-14, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the drawings:

pages 1/6-6/6, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-14	YES
	Claims		NO
Inventive step (IS)	Claims	1-14	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-14	YES
	Claims		NO

2. Citations and explanations

The document numbering follows the sequence used in the search report.

US 5 658 975 (**D1**) describes a hot-melt process for producing silicone pressure-sensitive adhesive compositions that contain an active substance. In addition to silicone, the matrix contains a siloxylated polyether wax (see claim 1). The matrix constituents and the active substance are homogeneously mixed at a temperature of 100°C and then cooled to ambient temperature (see examples 1-10 and column 7, lines 15-19).

EP 1 256 340 (**D2**) discloses a rotigotine-containing transdermal therapeutic system for treating parkinsonism (see paragraph [0001]). A solution of rotigotine base is prepared in ethanol, multiple adjuvants (for example, the crystallization inhibitor poly(vinyl pyrrolidone)) are added and the resulting product is worked into an amine-resistant silicone mixture dissolved in heptane (see paragraphs [0036]-[0037]). To remove the solvent, the matrix is dried over 30 min at a temperature of 80°C (see paragraph [0038]). The product contains

0.45 mg rotigotine/cm^2.

1) Novelty

The subject matter of claims 1-14 appears to be novel within the meaning of PCT Article 33(2) in light of the available citations.

2) Inventive step

The subject matter of claims 1-14 appears to involve an inventive step within the meaning of PCT Article 33(3) in light of the available citations.

The problem addressed by the application consists in providing a silicone-based transdermal system for delivering rotigotine which both enables the incorporation of a high content of active substance and is free of solubilisers, crystallization inhibitors and dispersants.

The solution proposed in the application is a matrix in which that part of the rotigotine not dissolved in the matrix polymer is contained as amorphous particles with a maximum size of 30 μm, said matrix containing only antioxidants in addition to the active substance.

D1 represents the closest prior art. Since the constituents are mixed at a temperature of 100°C (see column 10, lines 20-24), rotigotine would melt and thus inevitably be present as an amorphous product, as in the above-described process. Since a solvent is not used, it should likewise be possible to incorporate relatively large amounts of the

active substance. The formulation as per D1 deviates from the present application in that it comprises adjuvants other than antioxidants.

The formulation as per claims 1-7 and the production process as per claims 10-14 are neither described nor suggested by the available prior art

Therefore, the subject matter of claims 1-14 involves an inventive step.

3) **Industrial applicability**

The subject matter of claims 1-14 is industrially applicable within the meaning of PCT Article 33(4).